Dissertation on

CORRELATION OF HRCT WITH PFT AND BRONCHO ALVEOLAR LAVAGE IN INTERSTITIAL LUNG DISEASES OF COLLAGEN VASCULAR DISORDERS

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CERTIFICATE

Certified that this dissertation titled **"CORRELATION OF HRCT WITH PFT AND BRONCHO ALVEOLAR LAVAGE IN INTERSTITIAL LUNG DISEASES OF COLLAGEN VASCULAR DISORDERS"** is a bonafide work done by **DR.A.MAHESH KUMAR MD(TB&CD),** Post graduate student of Institute of Thoracic Medicine, Madras Medical College, Chennai, under the guidance and supervision of **PROF. R. ATHARUNISHA BEGUM, MD., DTCD.,** during the academic year 2003 – 2006.

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DECLARATION

I, **Dr. A. Mahesh Kumar**, declare that dissertation titled **"CORRELATION OF HRCT WITH PFT AND BRONCHO ALVEOLAR LAVAGE IN INTERSTITIAL LUNG DISEASES OF COLLAGEN VASCULAR DISORDERS"** is a bonafide work done by me at Institute of Thoracic Medicine, Chetput and Department Of Thoracic Medicine, Madras Medical College & Govt. General Hospital, Chennai-3 under the guidance of my Professor **Dr.R. Atharunnisa Begum M.D. (T.B. &C.D)**

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CONTENTS

INTRODUCTION

Interstitial lung diseases is a term given to a heterogeneous group of clinical entities that share the following features: dyspnea, hypoxemia, restrictive ventilatory defect and the presence of bilateral diffuse pulmonary infiltrates on the chest roentgenograms[1]. It is now recently called by the term Diffuse Parenchymal lung diseases (DPLD) which is now on an increase.

The reason for that is the increased awareness, thorough history evaluation and the lot of incoming trials in the field of investigating modality. The disease is characterized by deteriorating parenchymal fibrosis and gas exchange. It remains innocuous in the early stage as most of the rheumatic patients have restricted mobility manifesting with subtle or nil pulmonary symptoms. Hence respiratory physician should be prudential in diagnosing the cases as early as possible.

This study throws light on the semi invasive procedures on clinically and radiologically diagnosed cases rather than the invasive procedures. Since most of the patients denies procedures like surgical or transbronchial lung biopsies as well as they are in real respiratory

compromise, it is better to opt an alternative procedure. Bronchoalveolar lavage and pulmonary function test are frequently done nowadays as an adjunct to aid the diagnosis.

The extent and pattern of the lesion in the High resolution computerized tomography is described in detail and its severity is identified based on the correlation with PFT (Pulmonary function tests) and cellularity of the Bronchoalveolar lavage fluid. To enhance the knowledge in this area, statistical analysis is performed. This highlights the agreement as well as discordance between the variables.

AIM OF THE STUDY

To quantify the extent and severity of the interstitial lung disease as depicted in High Resolution computerized tomography.

To study the relationship between the radiological patterns of Interstitial lung diseases with functional parameter (Forced vital capacity) and the cellularity of bronchoalveolar lavage fluid in patients with collagen vascular diseases.

REVIEW OF LITERATURE

Interstitial lung diseases commonly complicates the management of connective tissue diseases (CTD). Hence a comprehensive understanding of the CTD and the usual course of Interstitial lung diseases (ILD) is important.

Approximately 15% of the patients who present with ILD have an underlying CTD[1]. Furthermore clinical symptoms like cough, dyspnoea may be the first manifestation of rheumatologic diseases. Finally it can result in significant morbidity and mortality.

The auto-immune mediated inflammation and fibrosis that characterizes these diseases can easily and irreversibly disrupt the normal functioning of the lung. As a group they can affect each portion of the lung: the pleura, alveoli, interstitium, vasculature, lymphatic tissue and of both small and large airways.

The lung diseases associated with collagen vascular disorder may precede the clinical presentation of collagen vascular disease by 5 years or more[1].

AUTOANTIBODIES ASSOCIATED WITH SPECIFIC COLLAGEN VASCULAR DISORDERS

DISEASES	ASSOCIATED ANTIBODIES
RHEUMATOID ARTHRTIS	RHEUMATOID FACTOR
PROGRESSIVE SYSTEMIC SCLEROSIS	ANTI-SCL -70 ANTI CENTROMERE ANTIBODY
MIXED CONNECTIVE TISSUE--DISEASE	ANTI RIBONUCLEAR PROTIEN
DERMATOMYOSITIS/ POLYMYOSITIS	ANTI-JO-1
SYSTEMIC LUPUS-- ERYTHEMATOSIS	ANTI-ds-DNA ANTI-sm
SJOGRENS SYNDROME	ANTI SS-A(Ro) ANTI SS-B(La)

Many of these diseases are characterized by the presence of the specific type of autoantibody which may greatly assist specific diagnosis.

Most of the parenchymal manifestations of Collagen vascular diseases are similar to idiopathic interstitial pneumonia.

RHEUMATOID ARTHRITIS:

It is a subacute or chronic inflammatory polyarthropathy of unknown cause that particularly affects peripheral joints. Lung fibrosis associated with the Rheumatoid arthritis (RA) was first reported by Ellman & Ball on 1948[2]. Two most common histological pattern observed are UIP & NSIP.

Rheumatoid lung fibrosis is twice as common in men as in women with a mean age of onset of about 50 yrs. Rheumatoid arthritis is characterized by the presence of symmetric arthritis, morning stiffness, and rheumatoid factor in the blood.

Pleuropulmonary complications are common and include interstitial pneumonitis and fibrosis, rheumatoid (necrobiotic) nodules, BOOP, bronchiectasis, obliterative bronchiolitis, follicular bronchiolitis, and pleural effusion or thickening [3,4].

Interstitial pneumonitis and fibrosis are the most common pulmonary manifestations of rheumatoid arthritis[3]. In fact, pulmonary function abnormalities consistent with interstitial fibrosis have been

reported in as many as 40% of patients who have rheumatoid arthritis[4]. In more than one-half of these patients, however, findings at chest radiography are normal. Evidence of interstitial fibrosis is seen at chest radiography in approximately 5% of patients with rheumatoid arthritis[3,5] and at high-resolution CT in 30%–40% [4,6]. The complication is seen most frequently in men between 50 and 60 years of age [7].

TYPES OF INTERSTITIAL PNEUMONIA:

Nonspecific interstitial pneumonia (NSIP)

Usual interstitial pneumonia (UIP)

Cryptogenic organizing pneumonia (COP)

Lymphocytic interstitial pneumonia (LIP).

The majority of patients who have interstitial fibrosis associated with rheumatoid arthritis have usual interstitial pneumonia; a small percentage have histologic findings of nonspecific interstitial pneumonia[7]. Nodular aggregates of lymphocytes may be prominent in both the parenchymal interstitium and in the interstitial tissue in bronchiolar walls and interlobular septa (follicular bronchiolitis) [8].

In one report, a variety of histopathologic features were seen in specimens obtained at open lung biopsy in patients with rheumatoid lung disease[8]. Five different groups were identified on the basis of histologic

patterns: pulmonary rheumatoid nodules, usual interstitial pneumonia, BOOP, lymphoid hyperplasia, and cellular interstitial infiltrates (nonspecific interstitial pneumonia). Few cases of diffuse alveolar damage have been reported [9].

Radiologic Manifestations

In the early stage, the radiographic appearance consists of irregular linear hyperattenuating areas in a fine reticular pattern. The abnormality usually involves mainly the lower lung zones. With the progression of disease, the reticular pattern becomes more coarse and diffuse, and honeycombing may be seen [10].

Similar to the findings at radiography, the predominant abnormality at high-resolution CT consists of irregular linear hyperattenuating areas caused by a combination of intralobular lines and irregular thickening of interlobular septa[4]. Honeycombing is seen, most markedly near the diaphragm.

In a study by Akira et al[11], three predominant CT patterns were identified in 29 patients: reticulation with or without honeycombing (*n* = 19), centrilobular branching linear structures with or without bronchial dilatation (*n* = 5), and consolidation (*n* = 5). Reticulation and centrilobular

branching linear structures corresponded to the histopathologic findings of usual interstitial pneumonia and BOOP, respectively. Consolidation corresponded to BOOP with or without findings of coexistent chronic eosinophilic pneumonia. Reticulation deteriorates rapidly, especially when it is associated with the new appearance of multifocal areas of ground-glass attenuation.

Centrilobular branching linear structures show a tendency to progress to bronchiectasis. Consolidation shows a tendency to improve in one-half of patients and to evolve into honeycombing in the remaining patients at serial CT.

Interstitial lung changes are frequent and independent of disease duration. Interstitial changes are more frequent and severe in rheumatoid factor–positive patients and in patients with more severe joint involvement[12].

PROGRESSIVE SYSTEMIC SCLEROSIS:

It is a generalized connective tissue disorder characterized by;

Tightening, induration & thickening of the skin (SCLERODERMA)

Raynauds phenomenon & other vascular anomalies.

Musculo-skeletal manifestations.

Visceral involvement particularly GIT, lungs, heart and kidneys

The lung is the fourth most commonly affected structure after skin, vessel and esophageal involvement[2]. The diagnosis can be made with high degree of certainity if the single major criterion of proximal scleroderma is present or if there are 2 or more minor criteria (sclerodactyly, pitting scars or loss of the substance of the finger tips or bilateral basal pulmonary fibrosis) [2].

PSS has 3:1 female to male distribution and presents more commonly in the 3rd -5th decade of life. Clinical syndrome of scleroderma may rarely occur in relationship with silicosis (ERASMUS SYNDROME).

High resolution computerized tomography findings in PSS have been described:

Ground glass opacification.

Fine reticular pattern (posterior and sub pleural).

Honey combing with sub pleural cysts.

Lines of various types (septal, sub pleural, long)

Sub pleural micronodules.

Lung fibrosis associated with the scleroderma holds much better prognosis than that found in IPF[2]. This is most likely due in part to the predominant NSIP histology. Progressive systemic sclerosis (scleroderma), an uncommon disease with an estimated incidence of approximately 10 cases per million per year, is a disorder of connective tissue characterized by deposition of excessive extracellular matrix and vascular obliteration [13].

Diffuse and limited forms of systemic sclerosis refer to the extent of cutaneous involvement, with a different clinical course and prognosis for each. Both types are more common in women, although the diffuse form tends to involve older women.

Pulmonary involvement is more common and more severe in systemic sclerosis than in other types of collagen vascular disease. The most common pulmonary manifestation is interstitial fibrosis, which occurs in approximately 80% of patients[13]. Pulmonary fibrosis is equally likely in the limited and diffuse forms of the disease but is less severe in the limited form.

Histopathologic Characteristics

At autopsy, some degree of parenchymal interstitial fibrosis is frequently seen. The histologic features are those of nonspecific or usual interstitial pneumonia, the former being more common. Follicular bronchiolitis is seen occasionally. Although BOOP may be associated with scleroderma, obliterative bronchiolitis is only rarely seen with the disease[14]. Diffuse alveolar damage has rarely been recognized in association with scleroderma[15].

Radiologic Manifestations

Evidence of interstitial fibrosis has been reported at chest radiography in 20%–65% of patients[13]. Serial radiographs obtained over several years may show progressive loss of lung volume in addition to a worsening of the interstitial disease.

High-resolution CT frequently shows evidence of interstitial pneumonitis and fibrosis in patients who have normal or questionable radiographic findings[16,17] . The abnormalities involve mainly the lower lobes and have a predominantly peripheral and posterior distribution[18].

In a recent study by Kim et al[19], findings at serial high-resolution CT were correlated with the results of pulmonary function tests in 40 patients with progressive systemic sclerosis and interstitial pneumonia. The overall

extent of disease and the degrees of honeycombing and ground-glass attenuation increased significantly at follow-up CT.

Both forced vital capacity and forced expiratory volume in 1 second decreased significantly at follow-up. The increase in the extent of honeycombing at CT correlated significantly with the decrease in diffusing capacity for carbon monoxide. The average rate of progression of honeycombing in patients with idiopathic usual interstitial pneumonia is 0.4% of lung volume per month[20]. According to study by Kim et al[19]the progression rate of honeycombing in patients with progressive systemic sclerosis is 0.07% of lung volume per month.

SYSTEMIC LUPUS ERYTHEMATOSUS

It is a multisystem collagen vascular disorder that particularly affects vessel, serosa, joints, kidneys, CNS, skin and blood vessels. The overall prevalence rate of SLE is about 20-50 cases per 10^5 population and it is 10 times as common in women as in men, with an increased prevalence among relatives and blacks[2]. The illness characteristically shows relapses and remissions and it presents typically in women of childbearing age with a wide variety of manifestations, particularly those of joint, skin (malar rash, photosensitivity, livedo reticularis), and systemic disorders.

Thoracic involvement is common in SLE, and the lungs, pleura, heart, diaphragm, and intercostals muscles may all be affected. Thoracic manifestations can be divided into primary changes or secondary complications.

Pulmonary manifestations of systemic lupus erythematosus comprise both acute and chronic lesions. Acute disease includes pulmonary hemorrhage, acute lupus pneumonitis, and pulmonary edema. Chronic disease, such as interstitial pneumonitis and fibrosis, is less common than in other connective tissue disorders [21].

SUBACUTE OR CHRONIC INTERSTITIAL PNEUMONIA

Nonspecific interstitial pneumonia.

Organizing pneumonia.

Usual interstitial pneumonia.

ACUTE LUPUS PNEUMONITIS

Acute lupus pneumonitis is characterized histologically by changes of diffuse alveolar damage (DAD). This is an unusual life-threatening condition characterized by acute onset of fever, cough, tachypnea, hypoxia, and radiologic consolidation and is a diagnosis of exclusion. It occurs in 1%–4% of patients[22,23]. Histopathologic findings include alveolar wall damage and necrosis that lead to inflammatory cell infiltration, hemorrhage, edema, and hyaline membrane formation .Large vessel vasculitis has rarely been detected. Thrombi in small vessels, associated with an interstitial pneumonitis, have been well documented, although this finding is an unusual feature of acute lupus pneumonitis. The pathogenesis of these histologic changes remains controversial [21].

PULMONARY FIBROSIS

Fibrotic interstitial lung disease is generally regarded as an unusual manifestation of SLE. A numerous patients with lung fibrosis have had preceding acute pneumonitis and the interstitial changes presumably

represent the organizing phase of DAD. Interlobular and intralobular lines were the most common type of abnormality. The most common signs were thickened interlobar septa, parenchymal bands, subpleural bands, and pleural tags and thickening.

Systemic lupus erythematosus is characterized immunologically by the presence of autoantibodies against various nuclear antigens. Pleuropulmonary involvement occurs in approximately 50%–60% of patients. Most such involvement consists of pleural disease[23]. In one prospective study that included 1,000 patients, lung involvement was identified in only 3% at the onset of the disease; it developed in an additional 7% over the period of observation[24].

Radiologic Manifestations

Ground-glass attenuation and consolidation at high-resolution CT may reflect the presence of interstitial pneumonitis and fibrosis, acute lupus pneumonitis, hemorrhage, or, occasionally, BOOP. Radiographic evidence of interstitial fibrosis, consisting of a reticular pattern that involves mainly the lower lung zones, is seen in only about 3% of patients who have systemic lupus erythematosus.

By contrast, interstitial abnormalities are seen in approximately 30% of patients at high-resolution CT[25,26]. They include interlobular septal thickening (33%), irregular linear hyperattenuating areas (33%), and

architectural distortion (22%). Such abnormalities are usually mild and focal; diffuse disease seen in only 4% of patients[22.] Honeycombing is uncommon.

POLYMYOSITIS / DERMATOMYOSITIS

They are diffuse inflammatory myopathies of striated muscle. Polymyositis is an autoimmune inflammatory myopathy characterized by symmetric weakness of the limb girdle and anterior neck muscles[27]. Additionally, in dermatomyositis there are characteristic skin changes. Female patients outnumber males by about 2:1. Polymyositis and dermatomyositis have an incidence of approximately 5–10 cases per million per year[27].

DIAGNOSTIC CRITERIA FOR POLYMYOSITIS AND DERMATOMYOSITIS

Proximal muscle weakness (Symmetric, present for weeks or months).

Muscle biopsy showing necrobiotic and inflammatory changes.

Raised muscle enzymes (Creatine phospohokinase).

Characteristic electromyography.

Characteristic skin rash.

In dermatomyositis, additional characteristic skin changes are present: Heliotrope periorbital rash and Violaceous / red papular rash

over bony prominences. Pulmonary involvement is quite common in polymyositis / dermatomyositis and may occur in up to 50% of patients.

The thorax is commonly affected, generally in one or more of three forms: (*a*) hypoventilation and respiratory failure as a result of involvement of the respiratory muscles; (*b*) interstitial pneumonitis, usually with a histologic pattern of usual interstitial pneumonia or nonspecific interstitial pneumonia; and (*c*) aspiration pneumonia secondary to pharyngeal muscle weakness (probably the most common pulmonary complication) [27,28].

INTERSTITIAL LUNG DISEASE

Interstitial fibrosis was first described in dermatomyositis in 1956 by Mills and Matthews. It is now a well recognized association that occurs in 5-10% of patients[2]. The presence of interstitial lung disease (ILD) in polymyositis / dermatomyositis correlates strongly with the presence of anti-Jo-1, a myositis specific autoantibody directed against a cellular enzymes (histidyl-t-RNA synthetase).

It is said that the ILD of polymyositis/ dermatomyositis is more steroid responsive than that of systemic sclerosis, perhaps due to a higher prevalence of OP[2].

Pathologic findings include: NSIP, OP, UIP (the frequency is less than in other collagen vascular disorders); DAD (which in the organizing phase is probably equivalent to AIP) vasculitis (small/medium vessel), primary pulmonary arterial fibroproliferative changes, diffuse pulmonary hemorrhage with capillaritis, and chronic eosinophilic pneumonia. More recent experience indicates that NSIP is more common than OP though a mixture of the two is frequent.

Radiographic changes commonly consist of symmetric basally predominant, reticulonodular opacity. The more acute cases may show areas of airspace opacity. In time, pulmonary changes can progress to involve the whole lung, and a fine honeycomb pattern.

The imaging findings depend on the type of histologic abnormality. In patients with histologic NSIP, ground-glass abnormality and reticular abnormality with traction bronchiectasis are the most common features, though consolidation may also occur. Pathologic correlation showed that patchy consolidation and ground-glass opacity was produced by OP, whereas extensive consolidation and ground-glass opacity indicated DAD. Honeycomb opacity is equated with UIP.

Histologic appearance is useful for determining the prognosis[28]. Patients with diffuse alveolar damage or usual interstitial pneumonia have a poor prognosis, with only a 33% survival rate at 5 years[29]. However, patients with BOOP have an excellent prognosis. Patients with nonspecific interstitial pneumonia have a good prognosis.

Radiologic Manifestations

The frequency of radiographic parenchymal abnormalities is low (about 5%). The most common is a symmetric, predominantly basal reticular pattern that may become diffuse over time and progress to honeycombing [27].

Bilateral areas of consolidation develop in some patients over a 2-3 week period. This abnormality usually corresponds histologically to diffuse alveolar damage or BOOP[28]. Initial high-resolution CT findings of pulmonary involvement in patients with polymyositis or dermatomyositis are prominent interlobular septa, ground-glass attenuation, patchy consolidation, parenchymal bands, irregular peribronchovascular thickening, and subpleural lines.

Honeycombing may be seen in up to 16% of patients who have abnormal chest radiographic findings or pulmonary function[30]. Areas of consolidation with or without ground-glass attenuation correspond histopathologically to BOOP or organizing diffuse alveolar damage. Patchy consolidation, parenchymal bands, and irregular peribronchovascular

thickening are seen to improve at sequential CT, becoming pleural irregularities, prominent interlobular septa, ground-glass attenuation, and subpleural lines on follow-up CT scans [31,32]. Therefore, consolidation with patchy and subpleural distribution, parenchymal bands, and irregular peribronchovascular thickening are reversible. On occasion, areas of ground-glass attenuation with parenchymal bands or subpleural lines that represent a pathologic area of usual interstitial pneumonia may progress to honeycombing [31].

SJOGREN SYNDROME

Sjogren syndrome (Sicca syndrome) is an autoimmune disorder characterized by clinical triad of dry eyes (keratoconjunctivitis sicca),dry mouth (xerostomia) and arthritis that particularly affects middle-aged females.

Pathologically, the hallmark of sjogren syndrome is widespread tissue infiltration by polyclonal B lymphocytes. It is relatively common, affecting 0.1% of the general population and 3% of older adults [33].It may be primary, without features of other collagen vascular disease, or secondary in association with other collagen vascular disease, most often rheumatoid arthritis.

EUROPEAN CLASSIFICATION CRITERIA FOR SJOGREN SYNDROME (FOUR OR MORE POSITIVE CRITERIA INDICATE PRIMARY SJOGREN SYNDROME) [2]**.**

Dry eyes.

Dry mouth.

Signs of keratoconjunctivitis sicca (Schirmer test and/or rose Bengal test positive).

Minor salivary gland histopathology- positive for focal mononuclear cell agglomerations.

Objective salivary gland involvement (one or more tests positive).

Salivary scintigraphy.

Parotid sialography.

Unstimulated salivary flow.

Antoantibodies (antibodies to Ro[SS-A] and / or La[SS-B]).

The pleuro-pulmonary manifestations of sjogrens syndrome reviewed by Caine et al falls in to 3 main groups.

Airway dryness, hoarseness & obstruction.

Lymphoproliferative

Manifestations of collagen vascular disorders.

The most common thoracic complication, lymphocytic interstitial pneumonia, is followed in frequency by airway abnormalities such as follicular bronchitis, bronchiectasis, and bronchiolitis. Less common complications include interstitial pneumonitis and fibrosis, BOOP, lymphoma, pulmonary hypertension, and pleural effusion or fibrosis [33] .

In the chest imaging, most of the common pulmonary manifestations particularly NSIP, UIP & LIP give rise to basal predominant nodular or reticulo-nodular shadows.

Radiologic Manifestations

Parenchymal abnormalities are evident at chest radiography in 10%–30% of patients[34]. The most common finding, a reticulonodular pattern that involves mainly the lower lung zones, may reflect the presence of lymphocytic interstitial pneumonia or interstitial fibrosis.

Franquet et al [35] made a prospective study of high-resolution CT findings in the lungs of 50 consecutive patients in whom the onset of disease occurred an average of 12 years prior to CT (range, 2–37 years). Moreover, 37 of 50 patients (74%) had no respiratory symptoms at the time of CT.

The authors detected abnormalities in 17 patients (34%) at CT and in only seven patients (14%) at chest radiography. The most common findings were bronchiolectasis and poorly defined centrilobular nodular or branching linear hyperattenuating areas (seen in 11 patients), (areas of ground-glass attenuation (seven patients), and honeycombing (four patients). Honeycombing alone or both honeycombing and ground-glass attenuation suggestive of pulmonary fibrosis were bilateral, asymmetric, and present almost exclusively in the periphery of the lower lobes.

OVERLAP SYNDROME AND MIXED CONNECTIVE TISSUE DISORDER

Some patients have an illness with the characteristic features of more than one connective tissue disorder; such patients are said to have an overlap syndrome or undifferentiated connective tissue disorder.

Mixed connective tissue disease (MCTD) is an overlap syndrome that is a distinct clinicopathologic entity. The principal characteristics are the presence of (1) features of SLE, systemic sclerosis, polymyositis / dermatomyositis, occurring together or evolving sequentially during observation and (2) Antibodies to an extractable nuclear antigen (RNP). Respiratory involvement has been described in 20%–80% of patients. Common pulmonary abnormalities include interstitial pneumonitis and fibrosis, pulmonary hypertension, and pleural effusion[36].

Suggested clinical criteria for the diagnosis are (1) positive anti-RNP plus (2) Three or more clinical features – hand edema, synovitis, myositis, Raynaud phenomenon, acrosclerosis. After several years MCTD may transform into one of the classic collagen vascular diseases.

Histopathologic findings of pulmonary involvement in mixed connective tissue disease are classified into interstitial fibrosis and vascular changes. Interstitial fibrosis has the appearance of usual or nonspecific interstitial pneumonia. Typical vascular changes consist of bland intimal proliferation of the lung arterioles, plexogenic angiopathy, and chronic pulmonary emboli [36].

In a review of the CT findings in 41 patients with MCTD, Kozuka et al found ground glass attenuation in all patients. Sub pleural micronodules, non septal linear and reticular abnormalities were all found in more than 50% of cases with CT pattern corresponding closely to NSIP.

The frequency of pulmonary abnormalities varies considerably in different series. For example, in a retrospective study of 81 patients at the Mayo Clinic [37], an interstitial pattern was seen at chest radiography in 19%; on the other hand, careful prospective study of 34 patients in another investigation[38], showed interstitial abnormalities in 85%. The abnormalities consist of irregular linear hyperattenuating areas with a reticular pattern

and involving mainly the lung bases. With the progression of disease, the fibrosis gradually extends superiorly; in the late stage, honeycombing may be identified. High-resolution CT shows a predominant subpleural distribution of fibrosis. Other radiologic abnormalities include areas of parenchymal consolidation that may be related to BOOP [39].

Radiologic Manifestations

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HIGH RESOLUTION COMPUTERISED TOMOGRAPHY FINDING IN ILD[40]

DIP &RB-ILD	SMOKING RELATED GROUND GLASS OPACITY & CENTRILOBULAR NODULES
LIP	GROUND GLASS OPACITY & PERIVASCULAR CYST
NSIP	BASAL GROUND GLASS & / RETICULAR PATTERN & TRACTION BRONCHIECTASIS
IPF(UIP)	BASAL & PERIPHERAL RETICULAR PATTERN + HONEY COMBING & TRACTION BRONCHIECTASIS
AIIP	DIFFUSE LUNG CONSOLIDATION & GROUND GLASS OPACITY

SPIROMETRY:

Spirometry is the measure of airflow during inspiration and expiration. It can be easily performed in the physician consulting room, with simple and affordable equipments called spirometer. The test is performed in sitting posture (by convention) and airflow is recorded as forced and sustained expiration followed by forced and sustained inspiration. 3 efforts, which have less than 5% and 100ml variability between each other, are selected and best effort is used for interpretation.

Routinely, only expiratory flow may be recorded before and after administration of bronchodilators. However both inspiratory and expiratory are required for evaluation of upper airway obstruction.

SPIROMETRY IS USEFUL FOR THE FOLLOWING:

- Evaluation of cases with respiratory symptoms.
- Assessment of severity of respiratory disorders.
- Assessment of response to therapy.
- Pre operative pulmonary evaluation.
- Detection of pulmonary abnormalities in predisposed individuals (e:g) occupational exposure, neuromuscular, chest wall or upper respiratory disorders.

SPIROMETRIC EQUIPMENT:

American Thoracic society (ATS) recommends that the equipment should be such that it meets the minimum standards i.e.

- Should record 7 litres volume and 12L/sec flow rate.
- Should be calibrated with a 3L syringe.
- Should record minimum FVC and FEV_1 and
- Should record flow volume curve or flow volume loop or both.

Subclinical interstitial lung involvement in rheumatic diseases was studied by Salaffi F and co workers. They correlated high resolution computerized tomography with functional and cytologic findings. Results of that Italian study is summarized below.

(41.2%) had abnormal High resolution computerized tomography findings. Chest X-ray showed parenchymal abnormalities in only 15 patients (18.7%) who had evidence of fibrosis on High resolution computerized tomography. Abnormal differential cell counts (alveolitis) at bronchoalveolar lavage were found in (57.5%). Three types of alveolitis were observed: pure lymphocyte alveolitis, pure neutrophil alveolitis, and neutrophil alveolitis associated with lymphocytosis (mixed alveolitis).

The patients with neutrophil alveolitis had more extensive disease on High resolution computerized tomography than those with lymphocyte alveolitis or with normal cellular patterns at bronchoalveolar lavage. The extent of a reticular pattern on High resolution computerized tomography correlated with the neutrophil rate ($p = 0.001$) and total count ($p = 0.003$) on bronchoalveolar lavage. Eosinophil and lymphocyte rate and total count correlated ($p < 0.05$) with the extent of the ground-glass pattern on High resolution computerized tomography. Lung volumes were not significantly different among patients with ground-glass pattern and those with reticular patterns on High resolution computerized tomography.

J. Biederer correlated High resolution computerized tomography findings, pulmonary function tests and bronchoalveolar lavage cytology in interstitial lung disease associated with rheumatoid arthritis and was published on line on 14 October2003. He found out that the High resolution computerized tomography appears most appropriate for the detection and follow-up of ILD associated with RA. The pulmonary function test and Bronchoalveolar lavage correlate only partially with lesion profusion or grading on High resolution computerized tomography, but they contribute valuable information about dynamic lung function.

Most of the DPLDs disclose a restrictive ventilatory pattern and low lung volumes in the pulmonary function tests (PFTs). However, some DPLDs may show obstructive patterns due to the bronchocentric nature of involvement; examples are sarcoidosis, chronic HSP, some presentations of rheumatoid arthritis, LAM, silicosis, allergic bronchopulmonary aspergillosis.

HIGH RESOLUTION COMPUTERISED TOMOGRAM:

In diffuse lung disease, it is generally accepted that the advent of high-resolution computed tomography (HRCT) has been the major diagnostic advance of the last 2 decades. High resolution computerized tomography is now an integral part of routine diagnostic evaluation, and its

use has had a major impact on the utility of other diagnostic tests, especially bronchoalveolar lavage and surgical biopsy procedures. However, as with all new diagnostic tests, the routine diagnostic application of High resolution computerized tomography has evolved slowly. The landmark diagnostic High resolution computerized tomography series were performed in the late 1980s and early 1990s but their extrapolation to clinical practice was largely confined to referral centers during that period[41].

The advantages and limitations of High resolution computerized tomography continued to be defined in subsequent series with a recent emphasis on the idiopathic interstitial pneumonias but histologic evaluation remained, for most clinicians, the diagnostic "gold standard" throughout the 1990s[41]. This view is increasingly questioned and it is now accepted that, in some contexts, High resolution computerized tomography evaluation obviates biopsy procedures.

This conclusion had recently been reinforced by the formulation of noninvasive diagnostic criteria for idiopathic pulmonary fibrosis (IPF). However, histologic assessment remains pivotal in other instances, and thus it is timely to explore the difficulties still faced by clinicians and radiologists in applying the diagnostic High resolution computerized tomography series to routine practice. The prevailing issue, pertaining to

referral and non referral populations alike, is the problem of extrapolating academic diagnostic series, containing large cohorts of patients with diffuse lung diseases, to individual patients.

Flexible bronchoscopy (FBS)

Flexible bronchoscopy (FBS) is an universally well accepted procedure both in the diagnosis and therapy of various pulmonary disorders. An experienced pulmonologist can perform this elegant procedure safely, follow the necessary precautions and increase the diagnostic yield in obscure respiratory diseases.

The birth of the bronchoscope was as early as 1897 when German laryngologist- Gustav Killian, "father of bronchoscopy" used a metal rod to remove an aspirated pork bone from a man's right main bronchus. Later in Philadelphia, Chevalier Jackson in 1904 modified the rigid bronchoscope (RB) with the addition of a direct ocular mechanism, suction tube and distal illumination.

The discovery of fiberoptics, that threads of glass could transmit light from one end to the other, can be traced back to 1870, but it was not until 1964 that this technology finally led Shigeto Ikeda of the National Cancer Institute, Tokyo, to develop the flexible fiberoptic bronchoscope.

RB until then was used to examine airways. Today there are two major types of bronchoscopes i.e. the rigid Jackson bronchoscope and the flexible fiberoptic bronchoscope (FBS). The flexible bronchoscope has

continued to gain utility primarily as a diagnostic tool. However, recently it has also become a popular modality for many therapeutic purposes.

BRONCHO ALVEOLAR LAVAGE:

It is the lavage of the bronchoalveolar secretions from the lower respiratory tract and is an important procedure that can be performed during bronchoscopy. This technique helps in the recovery of both cellular and non-cellular components from the epithelial surface of the lower respiratory tract and it differs from bronchial washings, which is usually an aspiration of secretions from the large airways. Hence Bronchoalveolar lavage can be called the 'liquid biopsy of the lung.

For Bronchoalveolar lavage the scope is wedged into the desired subsegmental bronchus of localised lung lesions or to the right middle lobe, in diffuse lung disease. 2-5 ml/kg of sterile, prewarmed normal saline in 3 equal aliquots are instilled through the port of the scope and subsequently aspirated back into specimen trap using suction. The specimens are labeled and transported to the laboratory immediately or within one hour in an ice container for bacteriological, cytological and immunological evaluation.

The normal cellular content of the Bronchoalveolar lavage fluid is

80% alveolar macrophages

10% lymphocytes

1-3% polymorphonuclear cells

1% eosinophil.

The ratio of CD4 T helper and CD8 T suppressor/ cytotoxic cells is about 1:5. In tuberculosis, sarcoidosis and hypersensitivity pneumonitis, Bronchoalveolar lavage shows lymphocytosis and there is neutrophilic predominance in interstitial pulmonary fibrosis.

In patients with AIDS and other immunodeficiency diseases Bronchoalveolar lavage is helpful in diagnosing opportunistic infections like pneumocystis carini, cytomegalovirus, aspergillus fumigatus, candida albicans, legionella pneumophilia and other pathogens. Bronchoalveolar lavage also plays an important role in the therapeutic management of alveolar proteinosis. Thus a high yield of meaningful clinically information can be expected from FBS when coupled with Bronchoalveolar lavage.

MATERIALS AND METHODS

The study was organized in the Institute of Thoracic Medicine (I.T.M) and Department of Thoracic Medicine in association with Rheumatology Department , Madras Medical College.

The design of the work is a prospective case study. It extends from the period of January 2005 to November 2005 and it is performed at the Department of Thoracic Medicine with source population from the Department of Rheumatology-Madras Medical College-Chennai.

INCLUSION CRITERIA

1). Serologically positive collagen vascular disorder patients.

2). Clinically and radiologically confirmed cases of Interstitial Lung Diseases (ILD).

EXCLUSION CRITERIA

1). Patient associated with co-morbid illness like congestive cardiac failure, tuberculosis and malignancy.

2). Smokers are virtually eliminated from the study since it is a confounding factor for (e:g) the respiratory bronchiolitis of

smoking can be falsely attributed to collagen vascular disorders.

3). ILD's due to other etiologies.

Granulamatous diseases

Environmental & occupational

Iatrogenic & drug induced

Idiopathic interstitial pneumonia

Unique entities

Inherited

4) ILD mimickers.

In essence without a medical history, all ILDs are of unknown cause. For an accurate diagnosis there is no substitute for complete clinical evaluation. This should be considered the key diagnostic step in the evaluation of patient who has ILD.

This includes a thorough history elicitation, with comprehensive evaluation of the chief complaint; a comprehensive review of multiple systems; identifications of all medications and drugs, including over the counter and naturopathic medications.

Then followed by exhaustive review of past medical, social, family and occupational histories with an exploration of all potential environmental exposures is done. The clues that surface during this evaluation helps to narrow the broad differential diagnosis to few possible disorders.

PULMONARY FUNCTION TEST (PFT):

After completing the physical examination of those who have full filled the criteria, were subjected to PFT. Before doing the PFT the various maneuvers of PFT were explained and practically demonstrated to them.

PFT was deferred to those persons who were suspected of having respiratory tract infection. A course of antibiotic was given for them and asked to come for the next session for the completion of PFT.

` PFT was done using MIR spirolab in which evaluation and interpretation of the values were made by comparing with specific predicted or normal values taken from a healthy population.

For all personnel FVC and FEV1/FVC were recorded and recorded values are taken as print out. One copy of the spirometry report was given to the person concerned for their reference.

AMERICAN THORACIC SOCIETY (ATS) RECOMMENDATIONS FOR PERFORMING THE SPIROMETRY[42]

Effort	:	Maximal, smooth and cough free.
Position	:	Sitting.
Exhalation time	:	6 seconds.
End of test	:	2 seconds volume plateau.
Reproducibility	:	FVC with in 5% in 3 acceptable tests.

HIGH RESOLUTION COMPUTERISED TOMOGRAPHY (HRCT)

The patients were then subjected to the High Resolution Computerized Tomogram (HRCT). The High resolution computerized tomography evaluation is done which includes characterization of pattern and profusion of the lesion on representative anatomical levels. High-resolution computed tomography (HRCT) has a central role in the routine detection and diagnosis of individual diffuse lung diseases.

BRONCHO ALVEOLAR LAVAGE (BAL):

It is also known as liquid biopsy or window of the lung. After a thorough history, clinical examination and pulmonary function tests, patients were subjected to Bronchoalveolar lavage.

Lung parenchymal evaluation by High resolution computerized tomography scanning of the chest has evolved to the point that it may provide images that are virtually diagnostic of certain forms of ILD but other tests like Bronchoalveolar lavage is required to secure an accurate diagnosis.

Bronchoalveolar lavage provides a safe and generally well tolerated means of retrieving secretions that coat the surface of bronchial and alveolar epithelium. Certain patterns of differential cell count correlate well with certain forms of ILD.

PROCEDURE:

The most important objective is to have adequate amounts of instilled saline reach the pathological sites that are involved by the disease so that the retrieved Bronchoalveolar lavage fluid reflects changes in cells and solutes caused by the inflammatory process.

100-200 ml of 0.9% prewarmed and buffered isotonic saline is instilled and 20ml aliquots are frequently employed. Middle / lingular lobe is the preferred site. Typically these sites are easily entered with the bronchoscope and the distal end of it can be wedged safely in segmental bronchi. Positioning the patient in such a way that the areas to be lavaged are not in the gravity dependent thereby it facilitates better retrieval of Bronchoalveolar lavage fluid.

Keeping the amount of negative pressure to a minimal level that allows retrieval of fluid prevents airway collapse unless advanced emphysema is present. Wall suction is applied with caution to generate negative suction pressure and kept at low value (25-100mm Hg). 50-80% of the instilled fluid is recovered.

Further samples are collected in a siliconised plastic container. Bronchoalveolar lavage fluid sample is immediately transported, filtered and centrifuged for 10 min at 500*g*. Counts are enumerated using cell smear technique and staining is done with Giemsa stain.

May - Grunwald (Giemsa) Staining Procedure

Purpose:

This standard operating procedure (SOP) establishes the standard for staining bacteria or mast cells using the May-Grunwald (Giemsa) staining procedure.

Reagents and Materials:

Jenner Solution

Giemsa Solution

Store at room temperature.

1% Acetic Acid

Acetic Acid	5ml
Distilled water	495ml

Materials

Specimen slides and control slides for special stain requested.

Microwave to bake slides.

Staining rack

Coverslips

Calibration and Standardization:

Procedure:

Deparaffinize and hydrate with distilled water.

Add Methanol for 6 minutes.

Then to add Jenner Solution (working) for 6 minutes.

Make fresh: Jenner Stain 20ml
Distilled water 20 ml

Then to add Giemsa Solution (working) for 45 minutes.

Make fresh: Giemsa Stain 1ml
Distilled water 50ml

Then to be rinsed with Distilled water , followed by

4 dips in 1% AceticAcid and to be rinsed with Distilled water

Dehydrate and clear it and then to apply coverslip.

Results:

Nuclei - blue

Cytoplasm - pink to rose

Bacteria or Mast Cells – blue

Statistical Analysis

Following statistical analysis are done to assess the strength of association between the variables of the study. They are

Student t-test

Chi-square test

Diagnostic statistics

Sensitivity

Specificity

Correct classification

Agreement statistics

Kappa statistics

McNemar's test

RESULTS

In our study 60 patients were screened for interstitial lung diseases. Out of which 55 patients were taken up for the study after satisfying the eligible criteria. Remaining 5 patients were excluded from the study group based on the exclusion criteria.

AGE:

In our study population, age ranges from 19yrs – 54 yrs (Fig 1).

AGE IN YEARS	NO. OF PATIENTS	PERCENTAGE
15-24	3	5.5
25-34	18	32.7
35-44	22	40
45-55	12	21.8
TOTAL	**55**	**100**

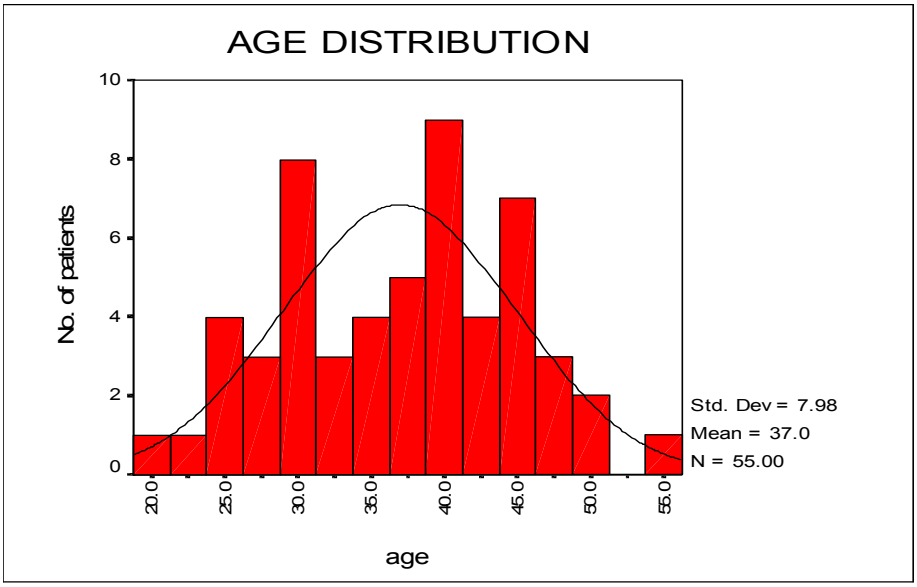

Fig 1. Age distribution.

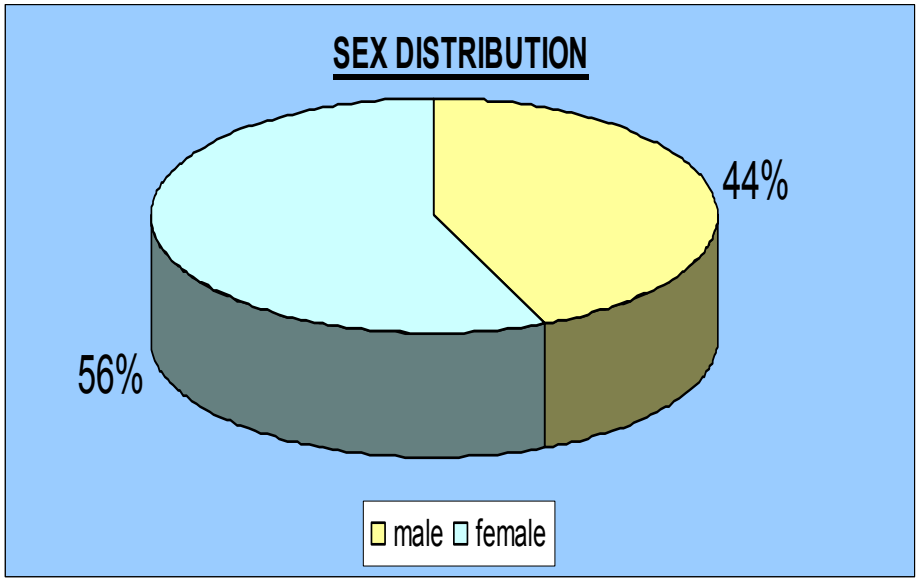

Fig 2. Sex distribution.

Maximum number of patients presented between the age of 25--44 years. Mean age distribution found in our study is 37. The calculated standard deviation is 7.98. Hence 95% of confidence interval lies in the age range of (37±15.96), indicating that the most of them falls in the late fourth decade.

SEX:

No. of males : 24

No. of females : 31

Male and female sex ratio (Fig 2) : 1:1.3

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SEX INCIDENCE OF DPLD IN RELATION TO COLLAGEN VASCULAR DISORDER

TYPES	FEMALE		MALE	
	NO	PERCENTAGE	NO	PERCENTAGE
RHEUMATOIDARTHRITIS	13	42	6	26
SYSTEMIC SCLEROSIS	8	26	12	50
SYSTEMIC LUPUS ERYTHEMATOSUS	4	13	1	4
POLYMYOSITIS/DERMATOMYOSITIS	3	10	1	4
SJOGRENS SYNDROME	2	6	2	8
OVERLAP SYNDROME	1	3	2	8
TOTAL	31	100	24	100

SEX RATIO FOR INDIVIDUAL COLLAGEN VASCULAR DISORDERS:

TYPES	SEX RATIO (M:F)
RHEUMATOIDARTHRITIS	1:2
SYSTEMIC SCLEROSIS	3:2
SYSTEMIC LUPUS ERYTHEMATOSUS	1:4
POLYMYOSITIS/DERMATOMYOSITIS	1:3
SJOGRENS SYNDROME	1:1
OVERLAP SYNDROME	2:1

CLINICAL FEATURES:

The pulmonary symptoms most commonly presented were non productive cough, breathlessness, chest pain and haemoptysis. Of this nonproductive cough was present in 49 patients (89.09%) followed by breathlessness in 41 patients (74.54%), chest pain in 17 patients (30.9%) and 4 patients (7.27%) with haemoptysis (Fig 3).

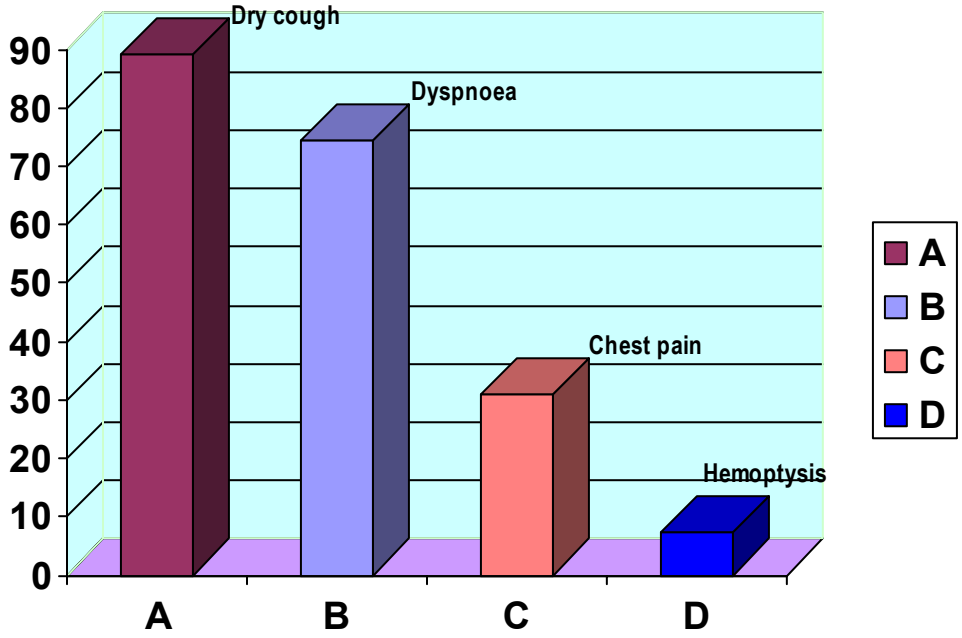

Fig 3. Pulmonary symptoms observed in the Interstitial lung diseases patients.

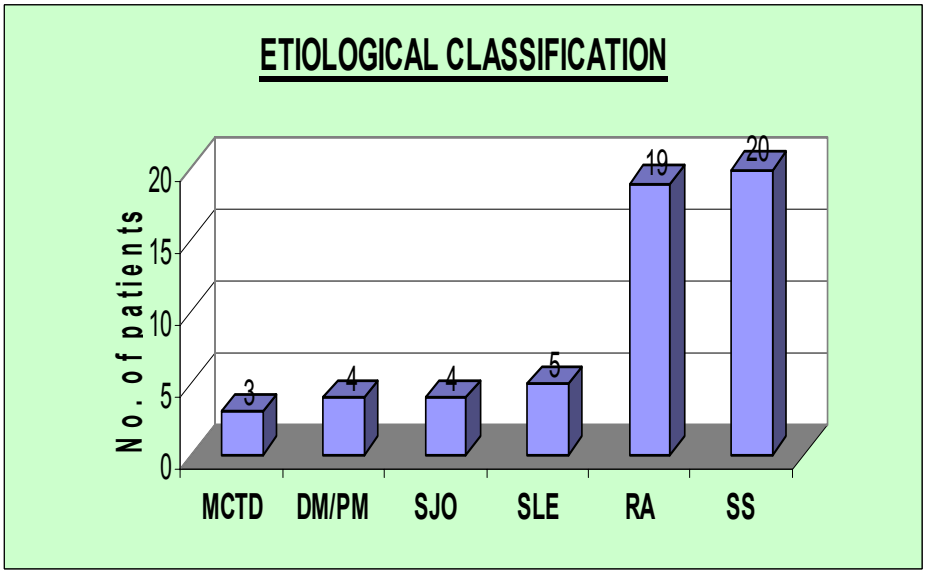

Fig 4. Aetiological classification of Interstitial lung diseases of collagen vascular disorders.

PULMONARY SYMPTOMS:

Symptoms	COLLAGEN VASCULAR DISORDERS											
	Systemic sclerosis		Rheumatoid Arthritis		Systemic Lupus Erythematosus		Sjogrens syndrome		Polymyositis/ Dermato--myositis		Overlap syndrome	
	No.	%	No.	%	No.	%	No.	%	No.	%	No	%
Dry Cough	19	95	18	94.7	3	60	3	75	4	100	2	66.7
Dyspnoea	17	85	14	73.7	4	80	3	75	2	50	1	33.3
Chest pain	4	20	7	36.8	3	60	1	25	1	25	1	33.3
Haemoptysis	-		1	5.3	2	40	1	25	-		-	

The predominant symptom found in majority of the study cases is nonproductive cough followed by breathlessness, chest pain and haemoptysis.

EXTRA PULMONARY SYMPTOMS:

Dyspepsia / Dysphagia / Raynauds phenomenon.

Inflammatory arthritis / subcutaneous nodules.

SICCA syndrome.

Skin lesions like rashes, discolouration and thickening .

Proximal muscle weakness.

These above mentioned extra pulmonary symptoms which is present concomitantly in our cases and these symptoms have preceded or accompanied with the respiratory illness.

	Frequency	Percent	Valid Percent	Cumulative Percent
DM/PM	4	7.3	7.3	7.3
MCTD	3	5.5	5.5	12.7
RA	19	34.5	34.5	47.3
SJO	4	7.3	7.3	54.5
SLE	5	9.1	9.1	63.6
SS	20	36.4	36.4	100.0
Total	55	100.0	100.0	

Rheumatoid arthritis and systemic sclerosis forms the bulk of the study population. It constitutes more than 70 % of the cases. Followed by 5 cases of Systemic lupus erythematosus and 4 cases each from Sjogrens syndrome and Dermato myositis / Polymyositis respectively and 3 cases from Mixed connective tissue disorder (Fig 4).

Chest x-ray showed parenchymal abnormalities only in 32 patients (58.18%) who had evidence of fibrosis on High resolution computerized tomography. Parenchymal abnormalities are in the form of reticular, nodular, reticulonodular and patchy ground glass opacity.

Cross tabulation of the chest x-ray and High resolution computerized tomography was done and their relationship were statistically analysed. Chest x-ray showed low sensitivity in diagnosing DPLD (diffuse parenchymal lung diseases) when compared to high resolution computerised tomogram. The efficiency of the chest x-ray is 58%. Though specificity is 98% the sensitivity is very low and marks only 58%. The kappa value is 0 indicating the discordance between chest x-ray and high resolution computerized tomogram in diagnosing ILD cases and the McNemar test showing the p value more than 0.05 indicating that there is no significant association.

HRCT patterns	**COLLAGEN VASCULAR DISORDERS**					
	Systemic sclerosis	Rheumatoid Arthritis	Systemic Lupus Erythematosus	Sjogrens syndrome	Polymyositis/ Dermato--myositis	Overlap syndrome
Reticular	19	18	3	4	4	2
Ground glass opacity (GGO)	1	1	2	-	-	1
Total	20	19	5	4	4	3

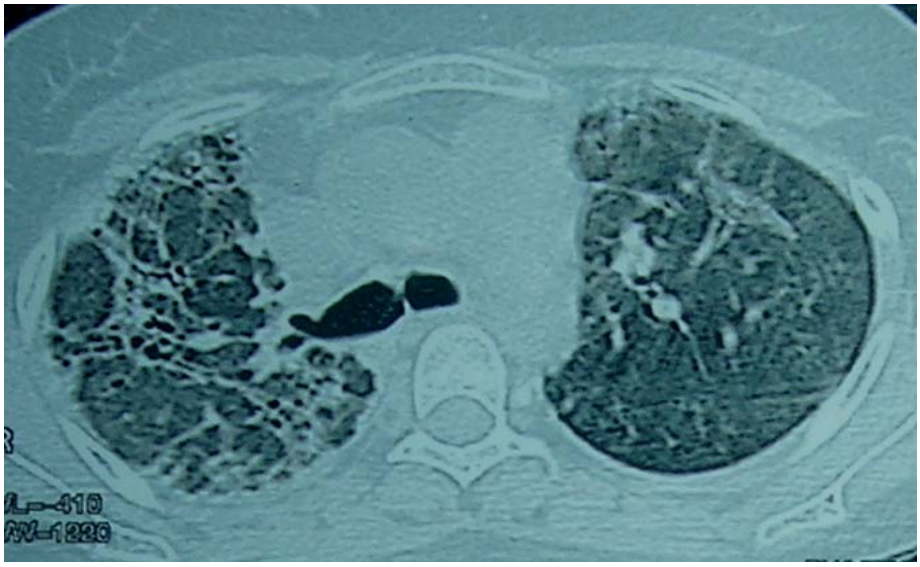

Fig5. Inter and Intra lobar septal thickening with traction bronchiectasis.

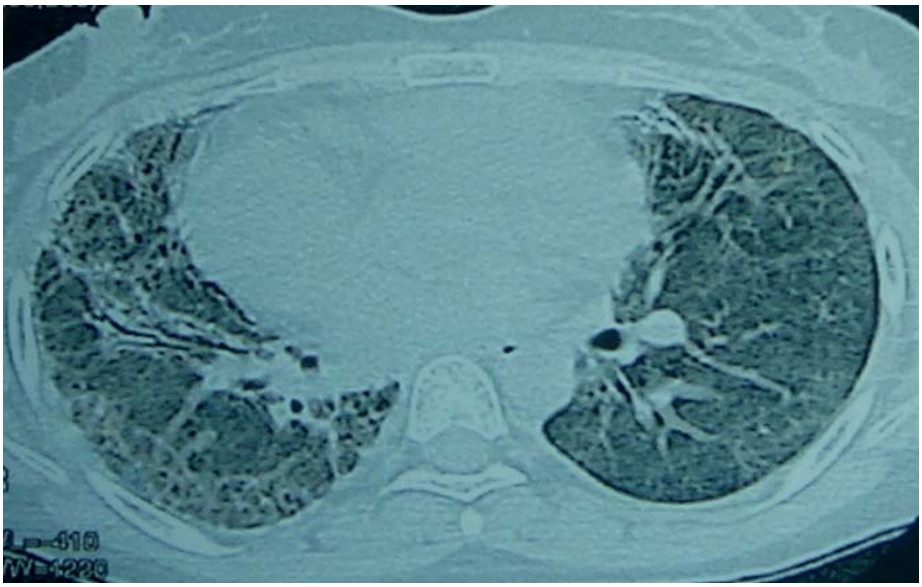

Fig 6. Bilateral sub pleural thickening and traction bronchiectasis more on the right side.

Reticular	50
Ground glass opacity (GGO)	5
Total	55

The frequently observed High resolution computerized tomography pattern is reticular (91%) (Fig 5, 6) and other is Ground Glass Opacity (9%) (Fig7,8). The profusion of lesion is variable but it predominated in the lower zone.

SITE OF LESION	NUMBER	PERCENTAGE
Lower zone	55	100
Mid and lower	26	47.27
Upper, Mid and Lower zone	7	12.73

HRCT Vs PFT

	PFT Pattern			TOTAL
	Normal	Restrictive	mixed	
HRCT				
Reticular	3	38(76%)	9	50
GGO	1	4(80%)	0	5
TOTAL	4	42	9	55

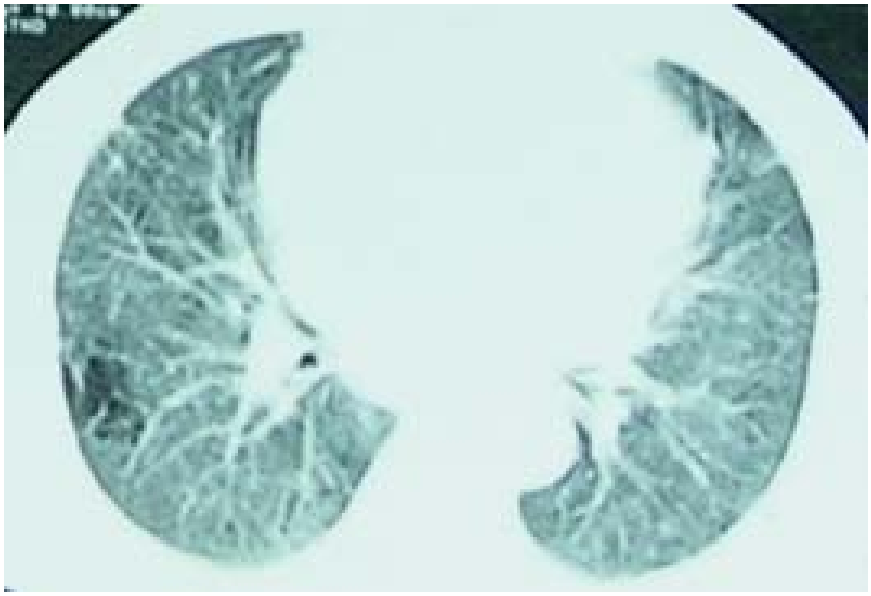

Fig 7. Bilateral diffuse Ground glass opacity.

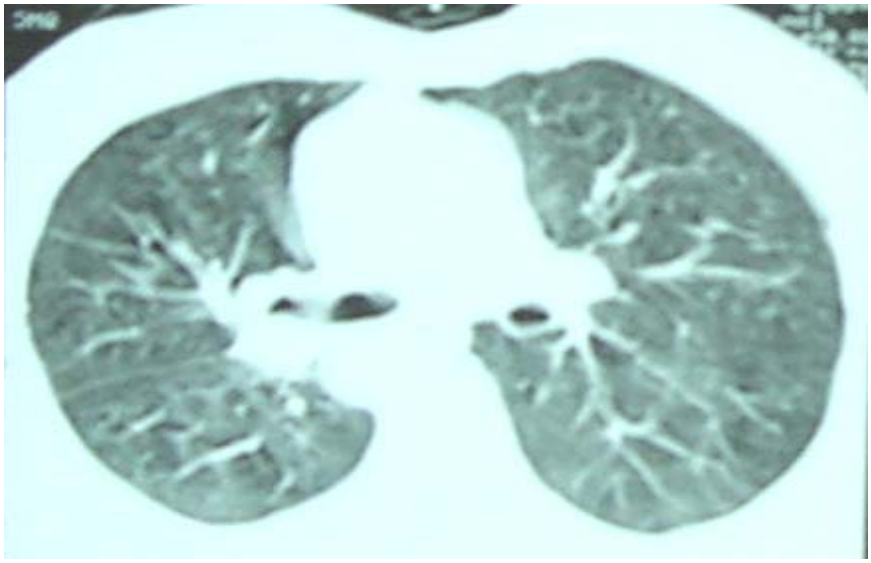

Fig 8. Bilateral diffuse Ground glass opacity.

HRCT (Reticular pattern) versus PFT (FVC)

Forced Vital Capacity (FVC) is uniformly reduced in both the High resolution computerized tomography patterns. Mean of FVC in reticular pattern is 2.54L with standard deviation of 0.175 (2.54±0.35). Similarly in Ground Glass Opacity pattern, the mean is 3.008L with standard deviation of 0.18 (3.008±0.36). Reticular pattern of High resolution computerized tomography is compared with the pulmonary function parameter of Forced Vital Capacity by using MIR SPIROLAB (Fig.10). The correct classification (efficiency) of the test is found to be 93%. The sensitivity is 90% and the specificity is 98%. Kappa score is 0.82 and p value is less than 0.001 indicating a good agreement. By McNemar test: $p < 0.001$ also a indicator of perfect agreement.

RETICULAR PATTERN

TYPES	No.	PERCENTAGE
Septal thickening (Inter / intra lobar)	32	64%
Sub pleural thickening	14	28%
Honey combing(Fig.9)	9	18%

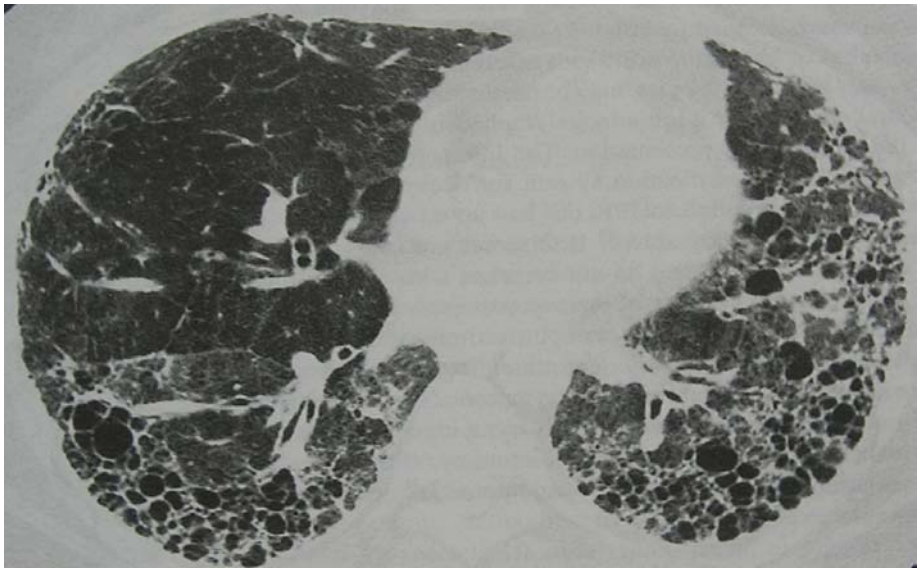

Fig 9. Honey combing – indicates the advanced stage of Interstitial lung diseases.

Fig10. MIR SPIRO LAB used for assessing the Pulmonary Functions.

HRCT Vs BAL

	HRCT			
	RETICULAR		GGO	
	n	%	n	%
BAL				
Normal	8	16%		
Neutrophilic	18	36%	1	20%
Lymphocytic	17	34%	2	40%
Mixed	7	14%	2	40%

HRCT (Reticular pattern) vesus BAL (Neutrophils)

Abnormal differential cell counts (alveolitis) at bronchoalveolar lavage were found in (76.66%) of the study group. Following types of alveolitis were found, pure lymphocytic, pure neutrophilic and mixed cellularity or with normal patterns. From the Bronchoalveolar lavage cellularity it is inferred that neutrophils and lymphocytes forms the bulk (70%) of the study (Fig.11&12) and almost equal contribution from each (35%). Reticular pattern of high resolution computerized tomography is compared with neutrophilic cellularity and statistically analysed. The correct classification (efficiency) of the test is found to be 98%. Sensitivity is 95% and specificity is about 97%. Kappa score of about 0.95 and p value less than 0.001 indicating a very good agreement.

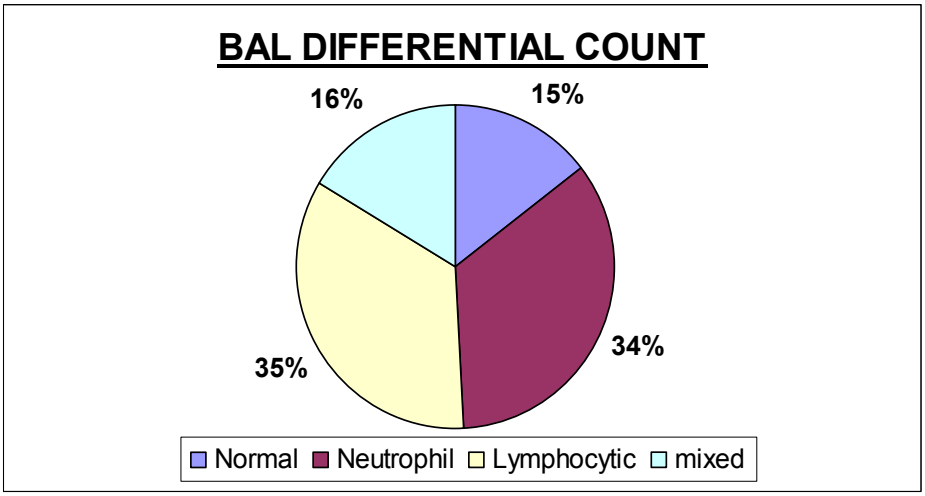

Fig11. Differential cell count of Bronchoalveolar lavage fluid.

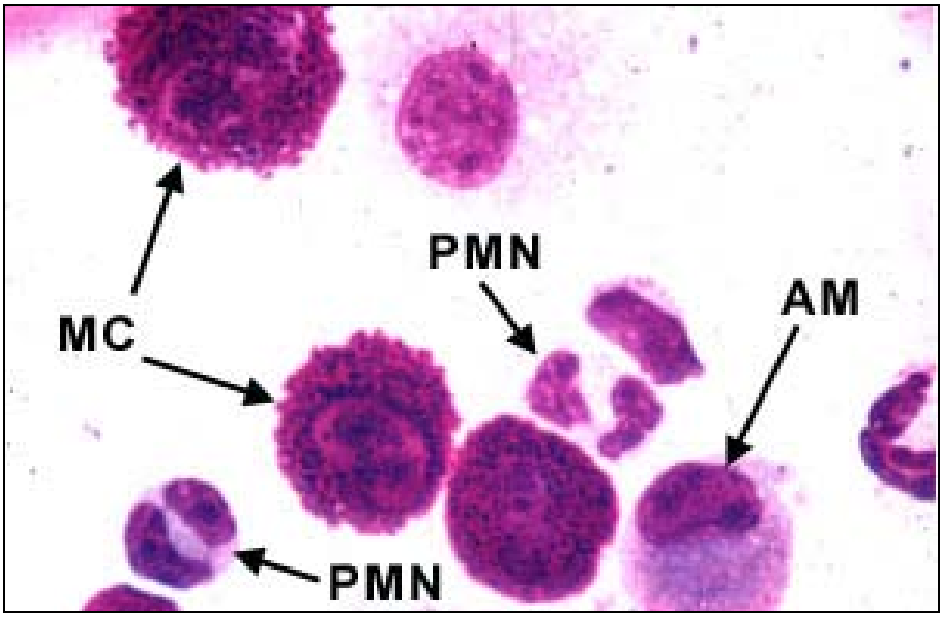

Fig12. Predominant neutrophils seen in the Bronchoalveolar lavage fluid.

DIAGNOSIS Vs BAL

BAL	DIAGNOSIS						TOTAL
	SS	RA	SJO	SLE	DM/ PM	MCTD	
Normal	3	4	0	0	1	0	8
Neutrophilic	8	7	0	2	1	1	19
Lymphocytic	5	7	4	0	2	1	19
Mixed	4	1	0	3	0	1	9
Total	20	19	4	5	4	3	55

The cellularity of Bronchoalveolar fluid identified from all the cases of Sjogrens syndrome is found to be lymphocytic predominance.

DISCUSSION

The study principally focuses on the characterization of the pattern and profusion of the radiological lesions and its severity is analysed by comparing with the pulmonary function (Forced vital capacity) and the cellularity of Bronchoalveolar lavage fluid.

Slight female predominance is noted in the incidence of Interstitial lung Diseases among collagen vascular disorder patients. The sex ratio favours female in systemic lupus erythematosus by 4 folds. MasiAt et al studied the sex effects in systemic lupus erythematosus-a clue to the pathogenesis published in Arthritis Rheum found to be 10 fold increase in the female sex incidence. Similarly females outnumber males in polymyositis / dermatomyositis and rheumatoid arthritis. The sex ratio is 1:3 and 1:2 respectively. It favours male sex in overlap syndrome and systemic sclerosis. The ratio is equal in sjogrens syndrome (1:1). There is not of much significant difference in sex wise age distribution as identified.

On the other hand comparing the chest x-ray with high resolution computerized tomography in our study, chest x-ray showed parenchymal abnormalities in (58.18%) who had evidence of fibrosis on High resolution computerized tomography. Abnormal differential cell counts (alveolitis) at bronchoalveolar lavage were found in

(76.66%). Following types of alveolitis were found, pure lymphocytic, pure neutrophilic, mixed cellularity and with normal patterns.

A study by Salaffi F and co workers about subclinical interstitial lung involvement in rheumatic diseases in which they correlated high resolution computerized tomography with functional and cytologic findings. Results of that Italian study indicates that the chest X-ray showed parenchymal abnormalities in only 15 patients (18.7%) who had evidence of fibrosis on High resolution computerized tomography. Abnormal differential cell counts (alveolitis) at bronchoalveolar lavage were found in (57.5%). Three types of alveolitis were observed: pure lymphocyte alveolitis, pure neutrophil alveolitis, and neutrophil alveolitis associated with lymphocytosis (mixed alveolitis). Patients with neutrophil alveolitis had more extensive disease on High resolution computerized tomography than those with lymphocyte alveolitis or with normal cellular patterns at bronchoalveolar lavage. The extent of a reticular pattern on High resolution computerized tomography correlated with the neutrophil of Bronchoalveolar lavage.

Hence it is inferred from the study that the High resolution computerized tomography is a highly sensitive tool in diagnosing Interstitial lung diseases (ILD /DPLD) of Collagen vascular disorder patients when compared to chest x ray. Predominant High resolution computerized tomography pattern identified from our study is Reticular rather than Ground glass opacity.

Neutrophilic cellularity of Bronchoalveolar lavage(BAL) is predominant in reticular pattern of High resolution computerized tomography and correlated well. Thereby it can predict the prognosis, as the response to steroids is weaker compared to the lymphocytic cellularity which is studied by Keith C Meyer et al and published in clin chest med sep 2004. All cases of Sjogrens syndrome had lymphocytic cellularity in Bronchoalveolar lavage suggestive of Lymphocytic interstitial pneumonitis.

Lower zone lesions are observed in majority of the cases compared to the mid and upper zones. Septal thickening is more frequently seen than honey combing. Irrespective of the High resolution computerized tomography pattern, most of them had reduced vital capacity. But the severity of reduction in Forced Vital Capacity is significant in Reticular compared to GGO(Ground Glass Opacity) pattern.

Bronchoalveolar lavage is broadly indicated in every patient with unclear diffuse lung disease. Nevertheless, Bronchoalveolar lavage has several advantages over biopsy procedures. It is safe and associated with virtually no morbidity. It collects sample from much larger area of the lungs than possible with biopsies. Hence it gives a representative picture of both inflammatory and immunological changes at an earlier date. So Bronchoalveolar lavage can be used as an adjunct along with clinical and radiological parameters in narrowing the differential diagnosis.

CONCLUSION

Majority of the cases (91%) were presented with the reticular pattern compared to the Ground Glass Opacity.

Both High resolution computerized tomography patterns (Reticular and Ground glass opacity) have reduced vital capacity but the severity of reduction is more in reticular pattern than that of the Ground Glass Opacity.

Of the reticular pattern inter / intralobar septal thickening is more frequent than either honey combing or sub pleural thickening.

The presence of Reticular pattern in High resolution computerized tomography has a very good correlation with reduced Forced vital capacity of the Pulmonary function test.

From the cross tabulation listed above and analyzing the Reticular pattern of high resolution computerized tomography with neutrophilic cellularity of Bronchoalveolar lavage, it is inferred from the values that there is a perfect agreement between these both.

Similarly the Ground Glass Opacity pattern has positive correlation with lymphocytic cellularity of Bronchoalveolar lavage.

So High Resolution Computerised Tomography is a sensitive tool in identifying pattern and profusion of the lesion. The severity of the lesion is identified by correlating High Resolution Computerised Tomography, pulmonary function and Bronchoalveolar lavage.

ABBREVIATIONS:

AIIP	**Acute Idiopathic Interstitial Pneumonitis**
BAL	**Broncho Alveolar Lavage**
BOOP	**Brochiolitis Obliterans Organising pneumonia**
CTD	**Connective Tissue Disorders**
DIP	**Diffuse Interstitial Pneumonitis**
HRCT	**High Resolution Computerised Tomography**
ILD	**Interstitial Lung Diseases**
LIP	**Lymphocytic Interstitial Pneumonitis**
NSIP	**Non Specific Interstitial Pneumonitis**
OP	**Organising pneumonia**
PFT	**Pulmonary Function Test**
RA	**Rheumatoid Arthritis**
RBILD	**Respiratory Bronchiolitis Interstitial Lung Diseases**
SLB	**Surgical Lung Biopsy**
TBLB	**Trans Bronchial Lung Biopsy**
UIP	**Usual Interstitial Pneumonitis**

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MASTER CHART

NAME	AGE	SEX	HRCT PAT	FVC(L)& % OF PRED	FEV1/FVC (%)	BAL	DIAGNOSIS
JEEVA	38	M	R	2.24(62%)	84	L	SS
PADMAVATHY	45	F	R	1.78(48%)	93	N	SS
LAKSHMIPATHY	45	M	R	2.67(64%)	101	M	RA
TIRUPURASUNDARI	40	F	R	2.45(61%)	66	L	RA
HARIDOSS	42	M	R	1.9(52%)	91	M	SS
VILVAKUMAR	54	M	R	2.11(54%)	82	NOR	RA
KALAISELVI	30	F	R	2.98(87%)	76	L	RA
EZHIL ARASI	45	F	R	2.52(56%)	106	N	RA
DEVI	32	F	R	1.61(49%)	111	N	SS
MURUGESAN	45	M	R	2.53(58%)	59	L	SS
MUNIAMMA	41	F	R	2.42(54%)	102	N	SLE
SAROJA	36	F	R	1.71(40%)	86	NOR	RA
VIJAYAKUMAR	30	M	R	2.29(56%)	83	N	SLE
DAMODHARAN	47	M	R	2.46((53%)	98	N	SS
CHANDRAMMA	32	F	R	2.64(50%)	94	M	SS
JAGADEESAN	31	M	R	1.43(44%)	97	M	SS
KASTURI	27	F	R	1.66(48%)	61	N	RA
PONNUTHAI	39	F	R	2.02(53%)	95	NOR	RA
VELU	43	M	R	2.35((56%)	107	L	RA
LAKSHMIPATHY	51	M	R	2.82(63%)	74	NOR	DM/PM
RAJESWARI	43	F	R	1.92(51%)	89	L	RA
CHINNAYA	37	M	R	1.8(46%)	93	NOR	SS
NAVANEETHAM	45	F	G	2.78(74%)	97	M	SLE
KUMARI	24	F	R	3.32(81%)	104	L	SS
SANKAR	29	M	R	3.67(72%)	63	N	SS
GUHAN	31	M	R	2.94(66%)	86	N	SS

BARATHI	37	F	R	3.04(69%)	93	N	RA
MAHESWARAN	41	M	R	2.85(58%)	48	L	SS
ANANDHI	25	F	R	2.39(59%)	102	NOR	RA
SAMPATH	33	M	R	3.52(69%)	106	M	SS
MANIMEGALAI	28	F	R	2.84(57%)	96	M	SLE
GOWRI SANKAR	42	M	G	2.67(54%)	110	L	RA
KOMALAVALLI	44	F	R	2.48(51%)	107	L	RA
USHA	39	F	R	3.31(68%)	94	NOR	SS
GOPAL	31	M	G	3.49(83%)	103	L	SS
THILAGAVATHI	26	F	R	3.39(69%)	95	L	DM/PM
RAMANI	37	F	R	2.89(63%)	88	NOR	SS
MALLIGA	19	F	R	2.78(61%)	73	L	DM/PM
SENTHIL	36	M	R	2.35(57%)	63	N	MCTD
EZHIL ARASI	40	F	G	2.34(51%)	87	M	SLE
NANDAKUMAR	31	M	R	2.63(63%)	81	N	RA
LEELAVATHY	46	F	R	2.07(56%)	59	N	RA
KRISHNAN	40	M	G	3.76(84%)	94	L	MCTD
VIMALA	37	F	R	1.78(40%)	86	N	SS
JAYANTHI	26	F	R	2.81(62%)	113	N	DM/PM
DEEPA	23	F	R	3.33(68%)	78	L	SJO
THAMILSELVI	34	F	R	2.45(64%)	89	N	RA
CHEVVEL	48	M	R	3.18(67%)	52	L	SJO
SEETHALAKSHMI	39	F	R	2.82(58%)	124	L	RA
VALARMATHY	47	F	R	1.61(39%)	73	M	MCTD
CYNTHIA	35	F	R	2.23(57%)	85	L	SJO
KARTHICK	29	M	R	3.48(84%)	96	N	RA
PARVATHY	50	F	R	2.31(54%)	105	N	SS
SABAPATHY	41	M	R	2.85(59%)	47	N	SS
KUMAR	27	M	R	3.21(68%)	84	L	SJO